

Sudden Cardiac Arrest in Childhood: An Overview

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Abstract

Sudden Cardiac Death (SCD) and Sudden Cardiac Arrest (SCA) are uncommon in childhood. The etiology is broad vary by age and may have a familial or genetic component. Although, SCD/SCA can occur without warning, a prodrome may be present. The primary care physician should be able to recognize "red flags" as investigation is essential. Further, models of preventive strategies are limited. We provide an overview of the epidemiology, etiology, risk stratification and prevention of SCA/SCD.

Introduction

Sudden cardiac death (SCD) is defined as "nontraumatic, nonviolent, unexpected event resulting from sudden cardiac arrest within six hours of a previously witnessed state of normal health" [1]. Sudden cardiac arrest (SCA) refers to an abrupt and unexpected loss of heart function that can cause SCD within minutes unless treated [2]. Despite, low incidence of SCA and SCD in childhood, once occurred, SCD has a profound and cascading effect on society including family members, communities and health care providers. We review the epidemiology and etiology of childhood SCD. We also highlight the early warning signs and discuss preventive strategies and future trends.

Epidemiology

The incidence of SCD in the pediatric population is estimated between 1-9/100,000 patient per year [3]. In the United States (US), Centers for Disease Control and Prevention estimated that approximately 1500 patients a year under the age of 25 will die from SCA [4]. An Italian study reported the incidence of SCA as 3.6 cases per 100,000 person-years among young competitive athletes before establishing a national screening program [5]. A prospective study from Australia and New Zealand showed an annual incidence of 1.3 cases per 100,000 of SCD among people between ages of 1-35 years. Further, a bimodal age distribution with peaks in infancy and adolescence and male predominance (72%) were documented [6]. A trends of incidence varied according to age, male predominance and ethnic background with white predominance (70%) [7]. It is still not clear whether athletic activity per se, without any underlying cause, may increases the risk for SCA/SCD [8]. While recent prospective study showed that most cases of SCD occurred during sleeping or resting rather than physical activity [6]. In contrast, other studies demonstrated increased risk for SCD/SCA with physical activity [5-7].

Etiology

The causes of SCA and SCD in the pediatric population are broad and vary by age with a significant familial/genetic factor. On the other hand, in many of the cases the etiology is unexplained [6]. Predisposing known cardiac pathologies is usually divided into 2 large groups. 1) Structural or functional – which can be identified by echocardiography/cardiac imaging/autopsy. 2) Electrical or primary arrhythmogenic disorders– which can be identified by an electrocardiogram (ECG) and in some cases by genetic/molecular testing. Among the most common structural etiologies are: A) Cardiomyopathies – including hypertrophic cardiomyopathy, dilated cardiomyopathy and Arrhythmogenic Right Ventricular Cardiomyopathy (ARVC). B) Coronary pathologies – both congenital, (i.e. coronary anomalies), and acquired (i.e. coronary artery atherosclerotic disease/ischemic heart disease). C) Congenital heart disease – such as tetralogy of Fallot, hypoplastic left heart, transposition of the great arteries, left ventricular outflow tract obstruction and others. This group includes also SCA/SCD as postoperative complications of congenital heart disease [9]. D) Myocarditis. E) Aortic anomalies – aortic dissection, aortic rupture connected to Marfan syndrome. F) Valvular – aortic stenosis and mitral valve prolapse. The most common electrical etiologies include: A) Long and short QT syndromes. B)

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Wolf-Parkinson-White (WPW) syndrome. C) Brugada syndrome. D) Catecholaminergic polymorphic ventricular tachycardia E) Complete heart block. Other recognized etiologies include primary pulmonary hypertension; cardiac tumors, chest wall trauma (commotio cordis) and some prescription medications [10]. The predisposing cardiac etiologies in the pediatric population for SCA/SCD vary with age. SCD in young children is more often associated with congenital heart disease while in older children and adolescents, arrhythmias and cardiomyopathies are more common [11].

Pediatric SCA/SCD Genetics

Many SCA/SCD etiologies both structural and electrical are known to be genetic [12-13].

Advances in cardiovascular genetics have added both molecular insight and new levels of complexity to our understanding of SCA/SCD [6,14,15,16]. Genetic testing for family members, and molecular autopsy (postmortem genetic testing for SCA/SCD etiologies) can be useful in identifying an etiology especially in cases where no etiology can be found even after an autopsy ("autopsy negative") [17-18].

Identification of Pediatric Population at Risk for SCA/SCD

Are there any "red flags" that can warn the primary care physician for a possibility of a potential future SCA/SCD event? Despite the fact that SCA can present without any preceding signs or symptoms. Studies of SCD/SCA showed that in many cases, prodromal symptoms, which sometimes are nonspecific, can present days or weeks prior to the SCA/SCD event and be misinterpreted by the primary care physician [19]. Those preceding factors can be in the form of patient reported symptoms, family history of SCA/SCD, abnormal findings in physical examination or abnormal ancillary tests such as an abnormal ECG (see table 1).

The most common signs and symptoms identified are history of syncope/presyncope, chest pain, palpitations, breathing difficulties/dyspnea on exertion and seizure like activity. The challenge facing primary care physicians is to differentiate those nonspecific and often benign complaints from an underlying cardiac pathology that puts the patient in risk of SCA/SCD. This differentiation requires a comprehensive medical history, physical examination, and testing if indicated.

Pre-Syncope/Syncope: The most common etiology of syncope in the pediatric population is neurocardiogenic syncope (also known as vasovagal syncope) [20]. Other common reasons are complex migraine headache, convulsion disorders and intracranial space occupation lesions. Most of these conditions accompanied by prodrome symptoms before the fainting event such as headache, dizziness, nausea, diaphoresis and visual changes. Vasovagal syncope has in many events an obvious trigger like positional changes, fear, pain and other body post situational changes (post micturition, post tussive etc.) In contrast, syncope from cardiac etiology connected to SCA/SCD occurs without warning, during exercise or in response to

auditory triggers and associated with chest pain and/or palpitations [21].

Chest pain: The most common cause for chest pain in the pediatric population is due to musculoskeletal conditions. Cardiac causes are uncommon cause of chest pain. Chest pain is almost never present in patients with primary electrical disorders but can appear in patients with structural defects such as cardiomyopathies, coronary abnormalities and aortic diseases [2]. Cardiac etiology for chest pain is more probable if the chest pain occurs during exertion, is recurrent, or if accompanied by palpitations or presyncope/syncope.

A thorough history and physical examination generally distinguish cardiac disease from benign conditions that do not require further work up. Cardiac evaluation is warranted in patients with abnormal physical findings or with cardio respiratory symptoms such as syncope, palpitations or dyspnea [22].

Palpitations: Palpitations among the pediatric population usually arise from non-cardiac physiologic stimuli such as fever, exercise and anxiety. Most common cardiac etiologies for palpitations are benign causes such as premature atrial and ventricular contractions rather than life threatening causes such as ventricular arrhythmias, cardiomyopathy and Myocarditis. In addition, children with series arrhythmias may report no palpitations. Children with a serious underlying cause often have a history of palpitations during strenuous exercise, syncope, congenital heart disease or cardiac surgery [23,24,25]. Those children should be placed in the emergency department on continuous cardiac monitoring and have 12 lead ECG done and warrant involvement of pediatric cardiology early in their evaluation.

Breathing difficulties/Dyspnea on Exertion: Most of the respiratory complaints among the pediatric population are non-cardiac like bronchiolitis, pneumonia, asthma. However, symptoms of dyspnea on exertion and exercise induced bronchospasm may be present in structural heart diseases and pulmonary hypertension. Failure to respond to empirical asthma treatment and normal pulmonary function test should warrant cardiovascular investigation.

Seizures: Cardiac electrical disorders such as Long QT associated with SCA/SCD may be short-lived and cause episodes of syncope and seizure like activity [26]. These phenomena may be difficult to distinguish from a seizure episode, one clue can be found in the fact that jerking movements in epilepsy begin simultaneously with posture lost and collapse while myoclonic movements due to cerebral hypoxia in SCA usually occurs after the initial collapse [27]. As a result, during investigation of a suspected seizure episode, one should maintain high index of suspicion and consider including an ECG and even echocardiogram.

Family History

Sudden, unexpected and unexplained death before the age of 50 in a family member can possibly be due to SCA. Retrospective studies

Personal Signs & Symptoms	Family History	Physical Examination	Diagnostic Test
Pre-Syncope /Syncope	SCA/SCD before the age of 50	Abnormal vital signs (Heart Rate, Blood Pressure, Pulse Oximetry)	Abnormal ECG findings (see details in table 2)
Chest pain	Known SCA/SCD predisposing cardiac condition	Physical stigmata of congenital anomalies	Abnormal chest x-ray (cardiomegaly, increased pulmonary vascular marking, pulmonary edema)
Palpitations	Drowning/Near Drowning	Abnormal heart sound /Pathologic murmurs	Abnormal echocardiogram
Dyspnea on Exertion	Congenital Deafness ¹	Others: Respiratory abnormalities, hepatomegaly, peripheral edema, poor perfusion	
	SIDS		

Table 1: Identification for pediatric patients at risk for sudden cardiac arrest/sudden cardiac death – List of potential warning signs

¹If not part of a known syndrome

showed affected individuals who experienced some antecedent symptoms also had a family history of SCA/SCD [28, 29].

Family history should also focus on cardiac etiologies associated with SCA/SCD such as cardiomyopathy, short and long QT syndrome, Brugada syndrome, Catecholaminergic ventricular tachycardia, ARVC, Marfan syndrome, Myocardial infarction at age 50 or younger, pacemaker or implanted defibrillator [2]. In families who are victims of SCA/SCD in one of the family members, a detailed family history should be obtained and a referral to a pediatric cardiologic and secondary testing include ECG, echocardiogram, exercise testing and genetic testing should be considered.

Other Conditions associated with SCA/SCD

Drowning or near drowning can be the result of cardiac arrhythmias such as Long QT [30]. Sudden infant death syndrome may be a result of a deadly arrhythmia as well [31]. Congenital deafness which is not associated with other recognized anomalies has been noted in some types of Long QT syndrome [32].

Abnormal Physical Examination

Abnormal physical examination findings that suggest an underlying cardiac disease can be coincidental findings that will trigger further cardiac investigation for SCA/SCD etiologies or part of focused physical exam due to other potential SCA/SCD “red flag” that have been discovered. Abnormal findings on physical examination that could point to SCA/SCD etiologies include 1-Abnormal vital signs such as: abnormal heart rate or rhythm, hypertension, respiratory rate and pulse oximetry. 2- Physical stigmata of congenital syndrome such as Marfan syndrome. 3- Abnormal Cardiac findings such as pathologic murmurs and abnormal heart sounds. Other findings that may suggest cardiac pathology are respiratory abnormalities, hepatomegaly, peripheral edema and poor perfusion.

Abnormal ECG findings

ECG is obtained in the pediatric population as part of the patient evaluation for concerning symptoms or as a screening test in many situations. Benign ECG findings are common in young people especially young athletes. (See table 2) Proper ECG interpretation that distinguishes physiologic adaptations from findings suggestive of an underlying cardiac pathology is essential to avoid unnecessary testing and parental anxiety. However, if ECG findings are deemed abnormal, further cardiac assessment and testing should be obtained.

Preventive strategies

Preventive strategies to reduce SCA/SCD can be divided into:

1. Primary prevention – “Screening”: Aims to identify the individuals at risk and to provide treatment options that would prevent SCA/SCD.
2. Secondary prevention – “Resuscitative”: Focused on successful resuscitation once SCA has occurred in order to improve survival rates and prevent poor outcomes.

Primary prevention

Various cardiovascular screening strategies for young athletes have been proposed. Current recommendations from the American Heart Association (AHA) and American Academy of Pediatrics (AAP) suggest that the most cost effective initial screening is detailed history and physical examination alone. The current data is lacking to recommend an optimal screening approach for primary prevention of SCA/SCD. However, the European Society of Cardiology (ESC) recommends a standard 12 lead ECG in addition to history and physical examination [33]. The ESC bases their recommendations of universal ECG screening for European athletes on the success of the Italian screening program. A study done in Italy has showed significant

Benign ECG Findings	Abnormal ECG findings	
	Finding	Definition
Sinus Arrhythmia	Tachyarrhythmias	Atrial – Supraventricular tachycardia, atrial-fibrillation, atrial-flutter Ventricular - Couplets, triplets and non-sustained ventricular tachycardia
Sinus Bradycardia	Profound sinus bradycardia	<30 BPM or sinus pauses ≥ 3 s
1° AV (Atrioventricular) Block	Pathologic Q waves	>3 mm in depth or >40 ms in duration in two or more leads (except for III and aVR)
Mobitz Type 1 - 2° AV (Atrioventricular) Block (Wenckebach)	QT abnormalities	Prolonged: QTc ≥ 450 ms (male), QTc ≥ 470 ms (female) Short: QTc ≤ 320 ms
Ectopic Rhythm	Wide QRS	QRS > 90 ms in children < 4 years QRS > 100 ms in children 4-16 years QRS > 120 ms in children >16 years
Junctional Rhythm	ST Segment Changes	ST elevation > 2 mm, ST depression > 0.5 mm in 2 or more leads,
IRBB (Incomplete Right Bundle Branch Block)	T waves inversion	>1 mm in depth in two or more leads V2–V6, II and aVF, or I and aVL (excludes III, aVR and V1)
Early Repolarization	Delta waves	Slurring of initial QRS and PR interval < 120 ms. Associated with Wolff Parkinson White (WPW).
Isolated criteria for LVH (Left Ventricular Hypertrophy) QRS	Brugada pattern	High take-off and down sloping ST segment elevation followed by a negative T wave in ≥ 2 leads in V1–V3
	Left axis deviation	-30° to -90°
	Left atrial enlargement	Prolonged P wave duration of >120 ms in leads I or II with negative portion of the P wave ≥ 1 mm in depth and ≥ 40 ms in duration in lead V1
	Right Ventricular Hypertrophy (RVH)	R–V1+S–V5 > 10.5 mm AND right axis Deviation >120°
	Premature ventricular contractions (PVC)	≥ 2 PVCs per 10 s tracing

Table 2: Benign and Abnormal ECG findings in Athletes

decrease in athlete's mortality from SCD after the implantation of a screening program which included a preparticipation ECG⁵. This could be due to the relatively high prevalence of cardiomyopathies such as ARVC in Italy [34]. At this point, more research needs to be done to determine the proper utilization of ECG in screening programs. In 2007, the AHA published the 12 elements (that later became the 14 elements) recommendations for preparticipation cardiovascular screening of competitive athletes which includes elements of personal history, family history and physical examination [35]. The AAP policy statement emphasized the importance of the following points for paediatric care providers for primary prevention of SCA: A) Recognize the warning signs and symptoms of SCA B) Obtain a comprehensive and accurate family history C) Use standardized preparticipation athletic evaluation to minimize unnecessary variation D) Refer any patient or family with known or suspected cardiac disorders to a paediatric cardiac center for further evaluation.

Impact of Screening Program

There are few data and no evidence based trial on the impact of screening programs on the incidence of SCD among athletes. There are no direct comparisons of the North America and European approaches to screening. Observational data are limited by the heterogeneity of both populations studied and screening protocols. While there are data that show improved outcomes with screening, the absolute benefit (based on the overall event rates) is small.

Follow up of Detected Abnormalities

The follow up evaluation of abnormalities detected depends on the specific abnormalities found or suspected. Patients with abnormal findings may require further evaluation such as echocardiography, exercise treadmill testing, Holter ECG monitoring, Cardiac Magnetic Resonance (CMR) genetic testing and referral to a pediatric cardiology specialist. Additional screening for first degree relatives should be obtained for patients with a diagnostic genetic disorder. In patients who have been identified as being high risk for SCA/SCD, an Implantable Cardiovascular Defibrillator (ICD) placement should be considered.

Secondary Prevention

Primary prevention programs alone can't prevent all SCA/SCD events. Low survival rates and poor long-term outcomes are related to prolonged periods of absent cardiac output. Both the AHA and the AAP support efforts to improve that by early symptoms recognition, use of emergency medical service teams, effective bystander cardiopulmonary resuscitation (CPR) and the use of automatic external defibrillators (AEDs) in the community. These statements emphasize the need for community support to place AEDs in public places, and to teach effective bystander CPR and AED use. High quality CPR has become apparent as the major determinant of survival [36] [37].

SCA Survivals and Victims

SCA survivals should complete a thorough investigation directed by a pediatric cardiologist which may include: echocardiogram, exercise treadmill testing, Holter ECG monitoring, Cardiac Magnetic Resonance (CMR) imaging and electrophysiologic (EP) were testing. For SCA survivors, part of secondary prevention may also include the placement of an ICD. First degree relatives should also be assessed and genetic testing should be considered. There are no consensus guidelines as to what postmortem investigation of a young SCD patient must entail or what the minimum premortem investigation of the first-degree relatives ought to include. Obtaining the phenotypic and genotypic information from the affected individual and close relatives should be considered in order to provide specific diagnosis, identify other family members at risk of SCA/SCD and provide clinical information of value to the survivors. If possible, a cardiac autopsy should be performed. If no cardiac anatomy explanation found a family screening and/or genetic testing as part of the evaluation are recommended.

Take Home Messages

1. Despite the fact that SCD/SCA can present without any warning signs, many children who experience SCA have prodromal suggesting history.
2. Alarming signs for SCD/SCA include symptoms such as syncope, chest pain, palpitations, seizure like activity and exertion dyspnea. Other alarming signs are family history of SCA/SCD < 50 years, abnormal physical examination and abnormal ECG findings.
3. The primary care physician should recognize those warning signs and direct those patients and families for additional testing.
4. The ideal screening approach for primary prevention of SCD is still uncertain. There is a consensus regarding using a detailed history and physical examination, while the uses of ECG for screening is still debatable.

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